

### **REMARKS**

Claims 1, 11, 13-17 and 37-48 are presently pending. Support for amendments to Claims 1, 11 and 13 is discussed below. Support for the amendments to Claim 37 and new claims 38-48 can be found in the Specification as filed as follows:

<b>Claim</b>	<b>Support in the Specification as filed</b>
37	Original Claim 11 and page 21, lines 9-14 of the Specification.
38	Original Claim 12.
39	Original Claim 1; and the Examples of the Specification.
40	Original Claim 1; and on page 12, line 13 to page 14, line 5; and on page 16, lines 17-35 of the Specification.
41	Original Claim 1, and in Example 1-1 and Table 1-1 of the Specification.
42	Original Claim 1, and in Example 1-1 of the Specification.
43	Original Claim 11; and on page 21, lines 9-14; and in Example 1-1 and Evaluation 1 of the Specification.
44	Original Claim 12, and in Example 1-1 and Evaluation 1 of the Specification.
45	Original Claim 11, and in the Examples of the Specification.
46	Original Claim 11; and on page 12, line 13 to page 14, line 5; and on page 16, lines 17-35 of the Specification.
47	Original Claim 11, and in the Examples and Table 1-1 of the Specification.
48	Original Claim 11, and in the Examples of the Specification.

No new matter has been added herewith. The following addresses the substance of the Office Action.

#### **Indefiniteness**

Claims 1, 11-17 and 37 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

Recitation of “an alkylene group” in claims 1 and 13 was found to be indefinite. In particular, the Examiner stated that it was unclear whether the term refers to a set of double bonded carbon atoms, only alkandiy groups, unsaturated and saturated alkane chains, or substituted or unsubstituted groups. Applicants have amended the term “alkylene” to “alkyl” throughout claims 1 and 13, thereby rendering the rejection moot. Support for this amendment is shown by the Examples, which disclose several compounds with alkyl groups. Thus, one of ordinary skill in the art would recognize that the term “aklylene” as formerly recited in the claims was intended to cover alkyl groups.

Recitation of "by one of formulae (11) to (17) in Claim 13 was found to be indefinite because it was unclear what formula (16) represents. The Applicants have amended Claim 13 to refer to formulae (11) to (15) or (17).

In view of the amendments to the claims, the Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

**Written Description**

Claims 1, 11-17 and 37 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. In particular, the Examiner stated that the specification does not disclose a representative number of species for the claimed genus of arbutin ester compounds as represented by formula (1), as defined in Claim 1. However, the scope of the claimed arbutin ester compounds and related methods of producing the compounds is specifically described, exactly as the compounds are claimed, with relevant, identifying characteristics, i.e., structural properties, in the Specification as filed at pages 5-11. Thus, the Specification provides ample written description of the claimed genus of compounds and related methods.

The Examiner stated that no representative examples are shown for an arbutin ester compound of formula (1) wherein Ra is R<sub>1</sub>-COOH and R<sub>1</sub>-COO-R<sub>2</sub> (see page 8, lines 1 to 2 of the Office Action). The Applicants have added new Claims 39 and 45, which limit Ra to -R<sub>1</sub>-CH=CH<sub>2</sub>, R<sub>1</sub>-C(CH<sub>3</sub>)=CH<sub>2</sub>, R<sub>1</sub>-COOCH=CH<sub>2</sub>, R<sub>1</sub>-C(CH<sub>3</sub>)<sub>3</sub>, to which this objection does not apply.

The Examiner also stated that the compounds reduced to practice are disclosed in Example 1-1 and Table 1-1, wherein R<sub>1</sub> in R<sub>1</sub>-C(CH<sub>3</sub>)=CH<sub>2</sub> and R<sub>1</sub>-C(CH<sub>3</sub>)<sub>3</sub> all represent a single bond, R<sub>1</sub> in R<sub>1</sub>-CH=CH<sub>2</sub> represents either a single bond or octyne group, and R<sub>1</sub> in R<sub>1</sub>-COOCH=CH<sub>2</sub> represents a butylene group (see page 7, lines 17 to 20 of the Office Action); and that the Specification discloses that the alkylene group has 1 to 16 carbon atoms (see page 7, lines 12 to 14 of the Office Action). The Applicants have added new Claims 40 and 46, which limit R<sub>1</sub> to a single bond or an alkyl group having 1 to 16 carbon atoms, to which this objection does not apply.

Further, the Applicants have added new Claims 41 and 47, which limit the compounds to those disclosed in Example 1-1 and Table 1-1; and Claim 42, which limits the compounds to 6-O-(10-undecenoyl)arbutin.

Notwithstanding the addition of these new claims, a written description is believed to be provided in Applicants' specification for all of the presently pending claims. The Applicants believe that the written description rejection is without basis for the following reasons:

- a) The specific definitions of R<sub>1</sub> and R<sub>2</sub> in the claims are clearly provided in the specification.
- b) The 13 compounds made and listed in Table 1-1, plus 6-O-(10-undecenoyl) arbutin, and related methods of making the compounds are given in Examples 1-1 to 1-5.
- c) As the Examiner noted at page 8 of the Office Action, the level of skill in the art and knowledge in the art is high, about that of a Ph.D. scientist with several years of experience. According to the Guidelines for Examination of Patent Applications under the Written Description Requirement, disclosure of fewer species is required to demonstrate that the Applicants were in possession of the claimed invention when the level of skill in the art is high.

Points (a) and (b) above are evidence that the applicants were in possession of the claimed scope of compounds and related methods. Regarding point (c), due to the high level of skill in the art, those of skill in the art would conclude that the Applicants were in possession of the claimed invention at the time the application was filed.

In view of the preceding remarks, the Applicants respectfully request that the rejections under 35 U.S.C. § 112, on the basis of lack of written description be withdrawn.

#### Enablement

Claim 11 was rejected under 35 U.S.C. § 112, first paragraph, because the Examiner alleged that the specification was enabling for a composition comprising 6-O-(10-undecenoyl) arbutin for inhibiting tyrosinase, but did not reasonably provide enablement for a composition comprising any compound of formula (1) for inhibiting tyrosinase. The Applicants have amended Claim 11 to recite a method of inhibiting tyrosinase comprising, providing as an active ingredient, at least one of the arbutin ester compounds according to claim 1, wherein tyrosinase is inhibited. Support for this amendment is found in the Specification as filed, for example at page 9, lines 6-8.

The Applicants have added dependent claims 45-48, which limit the compound of amended Claim 11. Dependent Claims 45 and 46 recite classes of compounds recited in Claim 1, and Claims 47 and 48 to recite the compounds listed in Table 1-1 and/or 6-O-(10-undecenoyl)

arbutin. The Applicants have also added claim 43, regarding a composition comprising 6-*O*-(10-undecenoyl)arbutin, and Claim 44 directed to an external preparation comprising the composition of Claim 43.

Notwithstanding the addition of the new compounds, the specification provides ample guidance to one having ordinary skill in the art that the compounds encompassed within the scope of amended Claim 11 would be useful in inhibiting tyrosinase. In particular, on page 26, lines 17-34, a description of the mechanism of action of the presently claimed compounds is provided. These mechanisms are further illustrated in Figures 5, 6 and 9, as described in that paragraph. One having ordinary skill in the art could readily determine that the use of compounds within the scope of Claim 11 could be used to accomplish these same mechanisms of action so as to inhibit tyrosinase as claimed. Accordingly, the full scope of Claim 11 is believed to be enabled by Applicants' specification.

In view of the amendments to the claims and the foregoing remarks, the Applicants respectfully request that the rejections on the basis of lack of enablement be withdrawn.

### **Anticipation**

Claims 1, 11 and 12 were rejected under 35 U.S.C. § 102(b) as being anticipated by Takido et al. (1983 *Phytochemistry* 22:223-225). Takido et al. disclose phlebotrichin, a phenolic glucoside. However, the compound disclosed by Takido et al. contains a hydroxyl group, which is not included in the compounds defined in Claim 1.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). “[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference.” *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). Since the compound of Takido et al. does not match the defined compounds in Claim 1, the reference does not anticipate the claims.

### **Obviousness**

Claims 13-17 and 37 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Takido et al. (supra), in further view of Weiss et al. (WO 2001/79241) in view of Kiyoshi et al. (JP 2001-151623). The Examiner stated that it would have been obvious to one of ordinary skill in the art to combine the teachings of Takido et al., concerning phlebotrichin, a phenolic

glucoside, with the teachings of Weiss et al., regarding biologically active glycoside esters of arbutin or other monosaccharides, with the teachings of Kiyoshi et al., regarding the preparation of a skin lotion.

However, in light of the remarks above, the compounds that are produced by methods claims 13-17 are novel. Weiss et al. and Kiyoshi et al. do not teach the presently claimed compounds, and fail to fill the gap between the present invention and Takido et al.

Moreover, the inventors have surprisingly shown that the claimed compounds demonstrate tyrosinase inhibitory activity. In particular, as described in Applicants' specification at page 26, lines 28-33, the claimed compounds exhibit inhibitory activity against both catechol and phenol substrates in contrast to arbutin itself. These unexpected results rebut any alleged *prima facie* obviousness with regard to all of the presently pending claims. Accordingly, the present invention as defined in the amended claims is not obvious over Takido et al. in view of Weiss et al. and Kiyoshi et al.

*No Disclaimers or Disavowals*

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

**CONCLUSION**

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Application No.: 10/530,789  
Filing Date: April 8, 2005

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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